## IN THE CLAIMS:

Cancel claims 1-15 and 30 without prejudice. Add the following new claims.

- 32. (New) A binding molecule which is a recombinant polypeptide comprising:
- (i) a binding domain capable of binding a target molecule, which binding domain is the binding site of an antibody, and
- (ii) an effector domain having an amino acid sequence substantially homologous to all or part of a constant domain of a human immunoglobulin heavy chain;

wherein the binding molecule is capable of binding the target molecule without triggering significant complement dependent lysis, or cell mediated destruction of the target, and capable of specifically binding FcRn and/or FcyRIIb,

and wherein the effector domain is a chimeric domain which is derived from two or more human immunoglobulin heavy chain C<sub>H</sub>2 domains, which human immunoglobulins are selected from IgG1, IgG2 and IgG4,

and wherein the chimeric domain is a human immunoglobulin heavy chain C<sub>H</sub>2 domain which has the following blocks of amino acids at the stated positions: 233P, 234V, 235A and 236G and 327G, 330S and 331S.

33. (New) The binding molecule as claimed in claim 32 wherein the effector domain is selected from  $G1\Delta ac$  or  $G4\Delta c$  as shown in Figure 17.



- 34. (New) The binding molecule as claimed in claim 32 wherein the effector domain is selected from GlΔac or G4Δc as shown in Figure 17 optionally comprising further amino acid substitutions or deletions to render the molecule substantially null allotypic.
- 35. (New) The binding molecule as claimed in claim 32

wherein the effector domain is derived from a first human immunoglobulin heavy chain  $C_{H2}$  domain wherein at least 1 amino acid in at least 1 region of the  $C_{H2}$  domain has been modified to the corresponding amino acid from a second, different, human immunoglobulin heavy chain  $C_{H2}$  domain, and

wherein the effector domain has a reduced affinity for Fc $\gamma$ RI, Fc $\gamma$ RIIa or Fc $\gamma$ RIII and a reduced ability to mediate complement lysis by comparison with the first or second human immunoglobulin heavy chain C<sub>H</sub>2 domain.

- 36. (New) The binding molecule as claimed in claim 35 wherein the effector domain has retained an affinity for FcyRIIb.
- 37. (New) The binding molecule as claimed in claim 32 wherein the binding domain derives from a different source to the effector domain.
- 38. (New) The binding molecule as claimed in claim 32 wherein the binding domain is capable of binding any of: the RhD antigen of red blood cells; an HPA alloantigen of platelets; a neutrophil antigen; a T-cell receptor; integrin; GBM collagen; Der P1; HPA-1a; VAP-1; laminin; lutheran; platelet glycoprotein VI; platelet glyprotein Ia/IIa.

- 39. (New) A binding molecule as claimed in claim 38 wherein the binding domain is selected from that of anti-CD52 antigen found on human lymphocytes; FOG1; OKT3; B2 (anti-HPA-1a); VAP-1; murine anti-α3 (IV) NC1; YTH12.5 (CD3); 2C7 (anti-Der p1); anti-laminin; or anti-lutheran.
- 40. (New) A pharmaceutical preparation comprising a binding molecule as claimed in claim 32 plus a pharmaceutically acceptable carrier.
- 41. (New) A binding molecule which is a recombinant polypeptide comprising:
- (i) a binding domain capable of binding a target molecule, which binding domain is the binding site of an antibody, and
- (ii) an effector domain having an amino acid sequence substantially homologous to all or part of a constant domain of a human immunoglobulin heavy chain;

wherein the binding molecule is capable of binding the target molecule without triggering significant complement dependent lysis, or cell mediated destruction of the target, and capable of specifically binding FcRn and/or FcyRIIb,

and wherein the effector domain is a chimeric domain which is derived from two or more human immunoglobulin heavy chain C<sub>H</sub>2 domains, which human immunoglobulins are selected from IgG1, IgG2 and IgG4,

and wherein the chimeric domain is a human immunoglobulin heavy chain  $C_{\rm H2}$  domain which has the following blocks of amino acids at the stated positions: 233P, 234V, 235A and no residue at 236; and 327G, 330S and 331S, and is at least 98%

identical to a C<sub>H</sub>2 sequence (residues 231-340) from human IgG1 or IgG2 having said modified amino acids.

- 42. (New) The binding molecule as claimed in claim 41 wherein the effector domain is selected from  $G1\Delta ab$  or  $G2\Delta a$ .
- 43. (New) The binding molecule as claimed in claim 41 wherein the effector domain is selected from  $G1\Delta ab$  or  $G2\Delta a$  optionally comprising further amino acid substitutions or deletions to render the molecule substantially null allotypic.
- 44. (New) The binding molecule as claimed in claim 41

wherein the effector domain is derived from a first human immunoglobulin heavy chain C<sub>H</sub>2 domain wherein at least 1 amino acid in at least 1 region of the C<sub>H</sub>2 domain has been modified to the corresponding amino acid from a second, different, human immunoglobulin heavy chain C<sub>H</sub>2 domain, and

wherein the effector domain has a reduced affinity for FcyRI, FcyRIIa or FcyRIII and a reduced ability to mediate complement lysis by comparison with the first or second human immunoglobulin heavy chain C<sub>H</sub>2 domain.

45. (New) The binding molecule as claimed in claim 44 wherein the effector domain has retained an affinity for FcγRIIb.

6 2003 15:27

ARMOUR et al. -- Serial No.: 09/674,857

- (New) The binding molecule as claimed in claim 41 wherein the binding domain 46. derives from a different source to the effector domain.
- (New) The binding molecule as claimed in claim 41 wherein the binding domain 47. is capable of binding any of: the RhD antigen of red blood cells; an HPA alloantigen of platelets; a neutrophil antigen; a T-cell receptor; integrin; GBM collagen; Der P1; HPA-1a; VAP-1; laminin; lutheran; platelet glycoprotein VI; platelet glyprotein Ia/IIa.
- (New) The binding molecule as claimed in claim 38 wherein the binding domain 48. is selected from that of anti-CD52 antigen found on human lymphocytes; FOG1; OKT3; B2 (anti-HPA-1a); VAP-1; murine anti-α3 (IV) NC1; YTH12.5 (CD3); 2C7 (anti-Der p I); anti-laminin; anti-lutheran.
- (New) A pharmaceutical preparation comprising a binding molecule as claimed 49. in claim 41 plus a pharmaceutically acceptable carrier.

## IN THE ABSTRACT:

Add the Abstract of the Disclosure submitted herewith on a separate sheet.

## REMARKS

Reconsideration of this application and entry of the foregoing amendments are respectfully requested.